AT

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/811,870	03/21/2001	Philip A. Cole	01107.00108	8634

22907 7590 04/29/2004

BANNER & WITCOFF
1001 G STREET N W
SUITE 1100
WASHINGTON, DC 20001

EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/811,870	COLE ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2004*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,58,60,63,66,67 and 69-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,58,60,63,66,67 and 69-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-15, 58, 60, 63, 66-67, and 69-76 are pending in the application.

[2] Applicants' amendment to the claims filed March 17, 2004, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicants' arguments filed on March 17, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[4] The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objections

[5] Claims 5-7 are objected to in the placement of commas following amino acids in the recited amino acid sequence. This may cause confusion as amino acid sequences are typically listed with hyphens and not commas separating the amino acids of a peptide sequence. In the interest of clarity, it is suggested that applicants place hyphens between the amino acids of the sequence.

Claim Rejections - 35 USC § 112, Second Paragraph

[6] In view of applicants' amendment to the claims, the rejection of claim 66 as set forth in item [7] of the Office action mailed November 17, 2003 is withdrawn.

[7] Claims 1-15, 58, 60, 63, 66-67, 69-71, and 74-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claims 1 (claims 2-14, 58, and 76 dependent therefrom), 15, and 60 (claims 63, 66-67, 69-71, and 74-75 dependent therefrom) are indefinite in the recitation of "the tether is ≥4.9 Å measured from a gamma phosphorous of the nucleotide or nucleotide analog moiety to the proton donor." While the specification discloses that the "[d]istance between the anilino nitrogen and the gamma-phosphorous was calculated using Chem3D assuming an extended conformation of the acetyl linker" (page 4, paragraph [17]), it remains unclear as to how a skilled artisan is to measure the distance "from a gamma phosphorous of the nucleotide or nucleotide analog moiety to the proton donor." The specification fails to identify how a skilled artisan is to perform such a measurement and by what means the measurement is to be taken. Is the measurement of a two-dimensional structure or of a three dimensional structure? And if the structure is three dimensional, is the measurement of a static structure or a conformationally flexible structure? And if a flexible three dimensional structure, is the measurement taken when the proton donor of the tether is farthest away for the gamma-phosphate, or can the measurement be taken when the molecule is conformed in such a way that the tether is closest to the gamma-phosphate? Moreover, it is noted that the specification indicates that nucleotide analogs may (and preferably) have "uncharged alkyl groups in place of one or more of the phosphate groups" (page 7, paragraph [27]; see also claims 8-9). Where the gamma phosphate is replaced by an alkyl group, it is unclear as to how a

skilled artisan is to measure the distance of the tether from the gamma phosphate, as no gamma-phosphate would be present in the molecule. As such, it is unclear as to the scope of the tethers that are to be included or excluded from the claimed bisubstrate inhibitors.

[b] Claim 15 recites the limitations "said insulin receptor kinase" in line 3 and "the bisubstrate inhibitor of insulin receptor kinase" in lines 6-7. There is insufficient antecedent basis for these limitations in the claim.

[c] Claim 66 is unclear in the recitation of "a nitrogen atom replaces a hydroxyl oxygen on a tyrosine". Based on its wording, the claim has been interpreted as referring to a tyrosine of the peptide moiety of the claimed bisubstrate inhibitor. However, there is no requirement that the bisubstrate inhibitor of claims 60 or 63 (from which claim 66 depends) comprise a tyrosine residue. It is suggested that applicants clarify the meaning of the claim – see for example, claim 4.

Claim Rejections - 35 USC § 112, First Paragraph

[8] Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. The claim recites the limitation "[a] bisubstrate inhibitor of insulin kinase". However, the examiner

can find no support in the specification, claims, or drawings as originally filed for a bisubstrate inhibitor of insulin kinase.

[9] The written description rejection of claims 1-14, 58, 60, 63, 66-67, and 69-76 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record (as set forth in item [8] of the Office action mailed November 17, 2003) and for the reasons stated below.

Applicants traverse the instant rejection by arguing that the specification provides a representative number of species of each of the component parts of the bisubstrate inhibitors, in addition to the actual reduction to practice of working examples. Applicants characterize the invention as comprising a nucleotide or nucleotide analog moiety, a peptide moiety that is a substrate for insulin receptor kinase or a protein kinase, and a tether that is greater than or equal to 4.9 angstroms when measured from a gamma phosphorous of the nucleotide or nucleotide analog moiety and a proton donor of the tether. Addressing the bisubstrate inhibitor of insulin receptor kinase (IRK) of claims 1-14, 58, 72, and 76, argue compound 2 (as shown in Figure 1 and at page 9 of the response) is a working example of the claimed genus. Applicants further argue the specification provides a representative number of nucleotide or nucleotide analog moieties (citing page 7, paragraph 27 of the specification). Applicants argue the specification provides identifying characteristics of the peptide moieties, which the specification allegedly teaches, has an amino acid sequence that is similar to the amino acid sequence of the natural protein substrate of IRK. Applicants argue the specification discloses SEQ ID NO:1 as a specific peptide moiety and that other peptides having

amino acid sequences of natural protein substrates of IRKs were well known in the prior art (citing the references of Shoelson et al. PNAS 89:2027-2031, Stadmauer et al. J Biol Chem 261:10000-10005, and Baron et al. J Biol Chem 273:7162-7168). Applicants argue the specification provides identifying characteristics of the tether (citing page 8, paragraph 29 and page 9, paragraph 31 of the specification) and cites a specific example thereof in Figure 1a. Applicants argue that the prior art knowledge of bond length combined with the specification's teachings that the tether can comprise carbon, hydrogen, and oxygen, and that it comprises a proton donor would demonstrate to a skilled artisan that applicants had disclosed a representative number of species of the tether. Applicants argue that even if the generic claims were not adequately described, claims 2-3, 5-7, and 71-72 are adequately described as these claims recite a specific nucleotide or nucleotide analog moiety, recite a specific peptide moiety, or recite a specific tether. Applicants' argument is not found persuasive.

The examiner maintains the position that the specification fails to describe the genus of claimed bisubstrate inhibitors of IRK as recited in claims 1-14, 58, 72, and 76. While the examiner acknowledges the disclosure of representative examples of nucleotides, nucleotide analogs, peptides, and tethers cited in the specification and prior art, it is noted that claims 1, 4, 8-14, 58, and 76 are not so limited to those cited representative examples. It is also noted that the peptide moiety of the inhibitor is not limited to a "natural substrate" of IRK. Instead, the genus of bisubstrate inhibitors of claims 1, 4, 8-14, 58, and 76 is essentially unlimited with respect to the structures and positioning of the nucleotide or nucleotide analog moiety, peptide moiety, and, in

particular, the tether that links these moieties. Moreover, each of the dependent claims (claims 2-3, 5-7, and 72) limits only a single feature of the bisubstrate inhibitor, while the other features remain unlimited. As such, the claims encompass species of bisubstrate inhibitors of IRK having widely variant structures. It should also be noted that applicants attempt to show possession of the genus of bisubstrate inhibitors of IRK by asserting that each of the components of the inhibitor is described in the specification or is well known in the art. However, even if all components of the inhibitor were described or known in the prior art (it is the examiner's position that they are not), this is no indication of possession of the claimed invention. For example, the components of DNA (the deoxynucleotides A, C, G, and T) are well known in the art, however, a claimed genus of nucleic acid sequences encoding a particular protein is not necessarily described merely because its individual parts, i.e., deoxynucleotides, are known. Furthermore, it is noted that the moieties of the inhibitor can be arranged or linked in any manner as they are not required to be linked as shown in compound 2. MPEP 2163 states, "[a] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes." The specification and the prior art fail to identify a "known or disclosed correlation" between the function of the compound, i.e., inhibition of IRK, and its structure. As such, the claims encompass species of bisubstrate inhibitors of IRK having widely variant structures. MPEP 2163 states, "[w]hat constitutes a "representative number" is an inverse function of the skill and knowledge in the art" and that "for inventions in

emerging and unpredictable technologies, or for inventions characterized by factors not reasonably predictable which are known to one of ordinary skill in the art, more evidence is required to show possession." The specification discloses only a single representative species of the genus of claimed bisubstrate inhibitors of IRK, i.e., compound 2 (see Figure 1a) and, based on this single disclosure, even in view of the teachings of the prior art, do not allow a skilled artisan to visualize the structures of all species encompassed by the genus of bisubstrate inhibitors of IRK. Thus, the single disclosed bisubstrate inhibitor of IRK fails to be representative of the entire genus.

Addressing the bisubstrate inhibitor of a protein kinase (PK) of claims 60, 63, 66-67, 69-71, and 73-75, applicants argue compounds 2 and 4 (as shown in Figures 1 and 4) are working examples of the claimed genus. Applicants further argue the specification teaches numerous suitable nucleotide or nucleotide analogs and provides identifying characteristics of the tether and a working example thereof. Applicants argue the specification describes two exemplary peptides – SEQ ID NO:1 and 2 – as specific peptide moieties and that other peptide substrates for other PKs were well known in the prior art (citing the references of Kwon et al. J Biol Chem 269:4839-4844, Marin et al. J Biol Chem 274:29260-29265, Onorato et al. J Biol Chem 270:21346-21353, Hutchins et al. FEBS Lett 466:91-95, Yamanashi et al. PNAS 90:3631-3635, Till et al. J Biol Chem 274:4995-5003, Garcia et al. J Biol Chem 268:25146-25151, and Silicia et al. J Biol Chem 273:16756-16763). Applicants argue that the prior art knowledge, the specification's teachings of identifying characteristics of the peptide and tether, and the specification's teaching of numerous nucleotide or nucleotide analogs, one would

conclude that applicants were in possession of the claimed invention. Applicants' argument is not found persuasive.

The examiner maintains the position that the specification fails to describe the genus of claimed bisubstrate inhibitors of a protein kinase as recited in claims 60, 63, 66-67, 69-71, and 73-75. While the examiner acknowledges applicants' representative examples of nucleotides, nucleotide analogs, peptides, and tethers cited in the specification and prior art, it is noted that claims 60, 63, 66-67, 69-71, and 74-75 are not so limited to those cited representative examples in the specification or prior art. Instead, the genus of bisubstrate inhibitors of claims 60, 63, 66-67, 69-71, and 74-75 is essentially unlimited with respect to the structures of the nucleotide or nucleotide analog moiety, peptide moiety, and, in particular, the tether. Moreover, dependent claim 73 limits only a single feature of the bisubstrate inhibitor, i.e., the tether, while the other features remain unlimited. It should also be noted that, with the exception of claim 63, the claims do not limit the type of PK that is inhibited by the bisubstrate inhibitor. It should also be noted that applicants attempt to demonstrate possession of the genus of bisubstrate inhibitors of PK by asserting that each of the components of the inhibitor is described in the specification or is well known in the art. However, even if all components of the inhibitor were described or known in the prior art (it is the examiner's position that they are not), this is no indication of possession of the claimed invention. Furthermore, it is noted that there is no indication in the claim as to the physical arrangement and linkage of the individual moieties of the inhibitor as they are not required to be linked as shown in compounds 2 and 4. MPEP 2163 states, "[a]

biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes." The specification and the prior art fail to identify a "known or disclosed correlation" between the function of the compound, i.e., inhibition of PK, and its structure. As such, the claims encompass species of bisubstrate inhibitors of PK having widely variant structures. MPEP 2163 states, "[w]hat constitutes a "representative number" is an inverse function of the skill and knowledge in the art" and that "for inventions in emerging and unpredictable technologies, or for inventions characterized by factors not reasonably predictable which are known to one of ordinary skill in the art, more evidence is required to show possession." The specification discloses only a two representative species of the genus of claimed bisubstrate inhibitors of PK, i.e., compounds 2 and 4 and, based on this disclosure, even in view of the teachings of the prior art, do not allow a skilled artisan to visualize the structures of all species encompassed by the genus of bisubstrate inhibitors of PK. Thus, the two disclosed bisubstrate inhibitors of PK fail to be representative of the entire genus.

Furthermore, it is noted that 69-71 and 74 recite the term "natural substrate." The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel* ,

984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). Also, MPEP § 2163 states (citing *Amgen*, 927 F.2d at 1206, 18 USPQ2d at 1021), "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials". In the instant case, the specification fails to identify those distinguishing characteristics of a genus of "natural" substrates of a protein kinase from those that are considered to be unnatural. In this case, the specification fails to define those structural features of a "natural substrate" of a protein kinase that are commonly possessed by members of the genus that distinguish them from other non-natural substrates. Thus, one skilled in the art cannot visualize or recognize the identity of the members of the genus. For the reasons stated above, the specification fails to describe all species encompassed by the genus.

[10] The scope of enablement rejection of claims 1-14, 58, 60, 63, 66, and 67 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record (as set forth in item [9] of the Office action mailed November 17, 2003) and for the reasons stated below.

Applicants traverse the instant rejection by arguing that each component of the bisubstrate inhibitor of IRK or PK was known in the art, citing Rosse et al. (Helvetica Chimica Acta 80:653-670) and Loog et al. (Bioorg Med Chem Lett 9:1447-1452) - it is noted that the reference of Loog et al. supra does not appear to have been made of record by applicants or the examiner and has not been provided by applicant for the examiner's review. Applicants address the Factors of In re Wands as follows: 1) nature

of the invention: applicants assert the nature of the invention is an improvement of bisubstrate inhibitors known in the prior art, i.e., specifying a dimension of the tether that represents the dissociative transition state; 2) state of the prior art: applicants assert the state of the art at the time of the invention was advanced, citing Shoelson et al. PNAS 89:2027-2031 and Sharma et al. J Biol Chem 274:9600-9606 as allegedly disclosing amino acid sequence motifs for substrates of IRK (Shoelson et al.), CDK5, and PKA (Sharma et al.); 3) the level of skill in the art: applicants assert that the level of skill in the art was high and that one of skill would have knowledge of bond lengths, PK substrate motifs, and substrate specificity; 4) level of predictability: applicants assert the level of predictability was high based on alleged numerous studies of PK substrates, knowledge of organic chemistry to make tethers, and knowledge of nucleotide moieties such that the components can be readily joined and no reasons have been set forth as to why the joined components should not function in the intended manner; 5) the amount of guidance: applicants assert the invention uses known components and that the length of the tether is all that is required to enable the invention; 6) working examples: applicants assert two working examples have been disclosed; 7) quantity of experimentation: applicants assert that to make the invention, one need only assemble the parts and that this assembly would not require undue experimentation. Applicants' argument is not found persuasive.

The examiner maintains the position that undue experimentation is required to make the full scope of the claimed invention. It should be noted that applicants fail to address the examiner's analysis of the Factors of In re Wands as set forth in a previous

Office action (see item [9] of the Office action mailed November 17, 2003) and are reiterated herein.

While applicants have failed to address the examiner's analysis of In re Wands, in the interest of advancing prosecution, applicants' arguments are addressed below. The examiner disagrees with applicants' assertion that each component of the bisubstrate inhibitor was known in the art. In this case, the broadest claims encompass a bisubstrate of IRK or PK comprising, any nucleotide analogs having any structure, including those yet to be isolated, any peptide substrate for IRK having any sequence and any number of amino acids, including those yet to be isolated, and a tether having an undefined structure (only that it comprise a proton donor and that it is ≥4.9 Å measured from a gamma phosphorous of the nucleotide or nucleotide analog moiety to the proton donor), wherein the moieties can be arranged in any manner as there is no limitation in the claims that would indicate where the moieties are physically linked (for example, the peptide moiety can be linked to the nucleotide at the 3' position of the ribose of the nucleotide). While representative components may have been known in the art at the time of the invention, the claims are not so limited to these representative components.

Regarding applicants' arguments addressing the nature of the invention, it is noted that the guidance provided by Rosse et al. supra relates to receptor tyrosine kinase bisubstrate inhibitors. It is noted that the reference of Loog et al. supra does not appear to have been made of record and has not been provided for the examiner's review. Nonetheless, there is no indication in the specification or the prior art that the

teachings of Rosse et al. supra, which address bisubstrate inhibitors of a receptor protein tyrosine kinase and Loog et al. supra, which address inhibitors of PKA, PKC, CDPK-1, CK1, and CK2, provide guidance for making a bisubstrate inhibitor for any protein kinase – particularly IRK. It should also be noted that neither of these references provides guidance for a tether as recited in the claims.

Regarding applicants' arguments addressing the state of the prior art, there is no dispute that the state of the prior art regarding substrates of IRK was advanced at the time of the invention. However, it is noted that the peptide substrates of the claim are not limited to those of the prior art, are not limited to those of IRK, and are not limited to those having the substrate motifs as disclosed in the prior art. The state of the prior art regarding *bisubstrate inhibitors* of any PK, particularly IRK, was certainly not well advanced. The instant invention is a combination of the three components and, while representative examples of a single component of that compound may have been known, this does not provide enablement for the full scope of the claimed invention, which as stated above, broadly encompasses a bisubstrate of IRK or PK comprising, any nucleotide analogs having any structure, including those yet to be isolated, any peptide substrate for IRK having any structure, including those yet to be isolated, and a tether comprising any proton donor that is ≥4.9 Å measured from a gamma phosphorous of the nucleotide or nucleotide analog moiety to the proton donor, wherein the moieties can be linked in any arrangment.

Regarding applicants' arguments addressing the level of skill in the art, while there is no dispute that a skilled artisan would have knowledge of bond lengths, protein

kinase substrate motifs, and substrate specificity of protein kinases, even a substantial amount of knowledge in these areas would not fully enable the claimed invention as the claimed bisubstrate inhibitors are not limited to those that have peptide substrates or nucleotide analogs that are known in the art and are not limited to any particular tether, only a tether having an unlimited length that is ≥4.9 Å measured from a gamma phosphorous of the nucleotide or nucleotide analog moiety to the proton donor.

Regarding applicants' arguments addressing the level of predictability, it is noted that the peptide substrate component and the nucleotide analog component of the claimed inhibitor is not limited to those of the prior art and the tether is not limited to those composed of carbon, hydrogen, and oxygen and, moreover, the length of the tether is unlimited. The specification fails to provide any guidance as to which substrates, nucleotide analogs, tethers and the ways in which the moieties are combined, i.e., physically linked, that are likely to provide the desired result. As such, it is highly unpredictable as to which of the numerous combinations is likely to provide a compound having the desired inhibitory activity.

Regarding applicants' arguments addressing the amount of guidance, it is noted that the peptide substrate and nucleotide analog components of the claimed inhibitor are not limited to those of the prior art. Furthermore, while the tether of the claimed inhibitor is limited to those that are ≥4.9 Å measured from a gamma phosphorous of the nucleotide or nucleotide analog moiety to the proton donor, the composition and length of the tether is unlimited and the specification fails to provide guidance for the

composition and/or length that is likely to result in a compound having the desired activity.

Regarding applicants' arguments addressing the amount of guidance, there is no dispute that the specification provides a single working example of the claimed IRK inhibitor and two working examples of the claims PK inhibitor. However, these two working examples fail to compensate for the lack of guidance in the specification.

Regarding applicants' arguments addressing the amount of experimentation, it is noted that the examiner disagrees with applicants' assertion that all components of the inhibitor were known. In this case, the broadest claims encompass a bisubstrate of IRK or PK comprising, any nucleotide analogs having any structure, including those yet to be isolated, any peptide substrate for IRK having any sequence and any number of amino acids, including those yet to be isolated, and a tether having an undefined structure, only that it comprise a proton donor and that it is ≥4.9 Å measured from a gamma phosphorous of the nucleotide or nucleotide analog moiety to the proton donor. It should be noted that there is no limitation in the claims that would indicate where the moieties are physically linked (for example, the peptide moiety can be linked to the nucleotide at the 3' position of the ribose of the nucleotide). While representative components may have been known in the art at the time of the invention, the claims are not so limited to these representative components. In this case, applicants would have a skilled artisan first experiment to identify all components as broadly encompassed by the claims and then experiment to determine the combination of components that has the desired activity. This clearly is not routine experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[11] Claim(s) 60, 67, 69-70, and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Ricouart et al. (J Med Chem 34:73-78; cited by applicants in the IDS filed March 20, 2002). The claims are drawn (in relevant part) to a bisubstrate inhibitor of a protein kinase comprising a peptide moiety and a nucleotide analog moiety linked by a tether comprising a proton donor, wherein the tether is ≥4.9 Å measured from a gamma phosphorous of the nucleotide or nucleotide analog moiety to the proton donor. As stated above, it is noted that the specification discloses that one or more phosphates of the nucleotide can be replaced by an alkyl group (page 7, paragraph [27]). The following rejection has been made in accordance with this definition. Ricouart et al. teach bisubstrate inhibitors of PKC comprising various ATP mimics having alkyl groups in place of the nucleotide phosphates, a substrate mimic, and a linker of multiple beta-alanine residues (page 74, Table I, compounds 2-3) that have the ability to bind and inhibit PKC and PKA (page 74, Table II). This anticipates claims 60, 67, 69-70, and 74.

Conclusion

[12] Status of the claims:

- Claims 1-15, 58, 60, 63, 66-67, and 69-76 are pending.
- Claims 1-15, 58, 60, 63, 66-67, and 69-76 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652

04-28-04